IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors : Alexander Gad and Dora Lis

Patent No. : 7,074,580

Issued : July 11, 2006

Serial No. : 10/792,311

Filed : March 2, 2004

Conf No. : 4992

For : COPOLYMER 1 RELATED POLYPEPTIDES FOR USE AS MOLECULAR WEIGHT MARKERS AND FOR THERAPEUTIC USE

30 Rockefeller Plaza
New York, New York 10112
November 19, 2010

Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

REQUEST FOR A CERTIFICATE OF CORRECTION UNDER 37 C.F.R. §1.322

Patentees enclose 1 sheet of Patent Office Form PTO/SB/44 (PTO-1050) indicating errors in the above-identified patent, attached hereto as **Exhibit A.** Patentees respectfully request that a Certificate of Correction under 37 C.F.R. §1.322 be issued for the above-identified patent.

Patentees maintain that the following errors are typographical errors which occurred through the fault of the Patent and Trademark Office and the corrections are clearly disclosed by the records of the Patent and Trademark Office.

The corrections are as follows:

Column 29, line 55, "$3x10^6$" should be changed to --$3x10^5$--. This correction is supported by applicants' July 18, 2005 amendment, page 3, line 7.

Column 30, line 60, "glutainic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 4, line 14.

Column 31, line 30, "glutainic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 5, line 2.

Column 33, line 9, "glutainic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 8, line 6.

Column 34, line 15, "glutaxnic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 10, line 14.

Column 34, line 50, "glutaxnic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 11, line 2.

Column 36, line 12, "glutarnic acid" should be changed to --glutamic acid--. This correction is supported by applicants' July 18, 2005 amendment, page 13, line 6.

Remarks

Patentees respectfully request that the Commissioner issue a Certificate of Correction under 37 C.F.R. §1.322 which provides for the correction of a "mistake in a patent incurred through the fault of the Patent and Trademark Office" which "is clearly disclosed by the records of the Office." Patentees maintain that each of the above errors is the fault of the Patent and Trademark Office for the reasons set forth below.

Specifically, the requested corrections are supported by applicants' July 18, 2005 Amendment, a copy of which is attached hereto as **Exhibit B**. In particular, claims 127, 131, 132, 143, 153, 154 and 163 of the July 18, 2005 Amendment recite the requested corrections.

In support of the correction requested, the undersigned, on behalf of patentees' assignees, requests that the Certificate of Corrections Branch review **Exhibits A** and **B** and issue the Certificate of Correction.

No fee is deemed necessary in connection with the filing of this Request for a Certificate of Correction. However, if any fee is deemed necessary, authority is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
30 Rockefeller Plaza
New York, New York 10112
(212) 278-0400

Certificate of Transmission

I hereby certify that this correspondence is being transmitted via the Electronic Filing System (EFS) to the U.S. Patent and Trademark Office on November 19, 2010.

11/19/10

Adam C. Krol Date
Reg. No. 64,351

PTO/SB/44 (09-07)
Approved for use through 08/31/2010. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,074,580

APPLICATION NO.: 10/792,311

ISSUE DATE : July 11, 2006

INVENTOR(S) : Alexander Gad and Dora Lis

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 29, line 55, "3x10^6" should be changed to --3x10^5--.

Column 30, line 60, "glutainic acid" should be changed to --glutamic acid--.

Column 31, line 30, "glutainic acid" should be changed to --glutamic acid--.

Column 33, line 9, "glutainic acid" should be changed to --glutamic acid--.

Column 34, line 15, "glutaxnic acid" should be changed to --glutamic acid--.

Column 34, line 50, "glutaxnic acid" should be changed to --glutamic acid--.

Column 36, line 12, "glutarnic acid" should be changed to --glutamic acid--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Cooper & Dunham LLP
30 Rockefeller Plaza
New York, NY 10112

EXPEDITED PROCEDURE Docket No. 2609/60807-AA-PCT-US/JPW/GJG/NDP
GROUP ART UNIT 1644
AMENDMENT UNDER 37 C.F.R. §1.116

IFW/AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Alexander Gad and Dora Lis
U.S. Serial No.:		10/792,311 Examiner: P. Huynh
Filed	:	March 2, 2004 Group Art Unit: 1644
For	:	COPOLYMER 1 RELATED POLYPEPTIDES FOR USE AS MOLECULAR WEIGHT MARKERS AND FOR THERAPEUTIC USE

1185 Avenue of the Americas
New York, New York 10036
July 18, 2005

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE UNDER 37 C.F.R. §1.116
TO JUNE 16, 2005 FINAL OFFICE ACTION

This is a response to the Final Office Action issued by the U.S. Patent and Trademark Office on June 16, 2005 in connection with the above identified application. A response to the June 16, 2005 Final Office Action is due September 16, 2005 and this amendment is timely filed.

In the Claims

Please amend the claims by replacing all prior versions, and listings, of claims pursuant to 37 C.F.R. §1.121(c) as follows:

1-122. (Canceled)

123. (Currently Amended) In a process for obtaining a pharmaceutical product containing a mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, wherein the mixture has an average molecular weight from 4000 to 13,000 Daltons and in the mixture the molar fraction of alanine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093 and wherein ~~during~~ the process includes determining the molecular weight distribution of a batch of ~~a~~ an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, ~~is tested~~ using a gel permeation chromatography column to determine whether the mixture has an average molecular weight from 4000 to 13,000 Daltons for inclusion in the pharmaceutical product, the improvement comprising

calibrating the molecular weight obtained using the gel permeation chromatography column by subjecting a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence, to chromatography on the column to establish a relationship between retention time on the column and molecular weight.

124-126. (Canceled)

127. (Previously presented) The process of claim 123, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2 x 10^6 Daltons, an optimal separation range of 1000 to 3x 10^5 Daltons, and a bead diameter of 20-40 μm.

128. (Previously presented) The process of claim 127, wherein the gel permeation chromatography column is Superose 12.

129. (Previously amended) The process of claim 123, wherein in the molecular weight markers the molar fraction of alanine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

130. (Previously Amended) The process of claim 129, wherein in the molecular weight markers the molar fraction of alanine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

131. (Previously presented) The process of claim 123, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

132. (Previously presented) The process of claim 123, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

133. (Previously Amended) The process of claim 123, wherein the pharmaceutical product is lyophilized.

134. (Previously Amended) A process for obtaining a pharmaceutical product containing a mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, wherein the mixture has an average molecular weight from 4000 to 13,000 Daltons and in the mixture the molar fraction of alanine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093, which comprises obtaining a batch of a mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine;

determining the average molecular weight of the mixture of polypeptides in the batch using a molecular weight-calibrated gel permeation chromatography column; and

including in the pharmaceutical product the mixture if the mixture is determined to have an average molecular weight from 4000 to 13,000 Daltons,

wherein the gel permeation chromatography column is calibrated by subjecting a plurality of molecular weight markers to chromatography on the column to establish a relationship between the retention time on the column and molecular weight, wherein each of the markers is a polypeptide consisting essentially of

alanine, glutamic acid, tyrosine and lysine and has a predetermined amino sequence.

135-137. (Canceled)

138. (Previously presented) The process of claim 134, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2 x 10^6 Daltons, an optimal separation range of 1000 to 3x 10^5 Daltons, and a bead diameter of 20-40 µm.

139. (Previously presented) The process of claim 138, wherein the gel permeation chromatography column is Superose 12.

140. (Previously Amended) The process of claim 134, wherein in the molecular weight markers the molar fraction of alanine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

141. (Previously Amended) The process of claim 140, wherein in the molecular weight markers the molar fraction of alanine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

142. (Previously presented) The process of claim 134, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

143. (Previously presented) The process of claim 134, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and

AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK
AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA
(SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

144. (Currently Amended) The process of claim 134, further comprising a step of lyophilizing the mixture ~~having the average molecular weight from 4,000 to 13,000 Daltons~~ of polypeptides.

145. (Previously Amended) A process for determining the average molecular weight of an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, wherein in the mixture the molar fraction of alanine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093, which comprises subjecting the mixture to chromatography on a molecular weight-calibrated gel permeation chromatography column so as to determine the average molecular weight of the mixture, wherein the gel permeation chromatography column is calibrated by subjecting a plurality of molecular weight markers to chromatography on the column to establish a relationship between retention time on the column and molecular weight, wherein each of the markers is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and has a predetermined amino acid sequence.

146-148. (Canceled)

149. (Previously presented) The process of claim 145, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2 x 10^6 Daltons, an optimal separation range of 1000 to 3x 10^5 Daltons, and a bead diameter of 20-40 µm.

150. (Previously presented) The process of claim 149, wherein the gel permeation chromatography column is Superose 12.

151. (Previously Amended) The process of claim 145, wherein in the molecular weight markers the molar fraction of alanine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

152. (Previously Amended) The process of claim 151, wherein in the molecular weight markers the molar fraction of alanine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

153. (Previously presented) The process of claim 145, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

154. (Previously presented) The process of claim 145, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

155. (Previously Amended) A process for determining whether an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, has an average molecular weight from 4000 to 13,000 Daltons, wherein in the mixture the molar fraction of alanine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093, which process comprises subjecting the mixture to a calibrated gel permeation chromatography column to determine the average molecular weight of the mixture wherein the gel permeation chromatography column is calibrated by subjecting a plurality of molecular weight markers to chromatography on the column to establish a relationship between retention time on the column and molecular weight, wherein each of the markers is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and has a predetermined amino acid sequence.

156-158. (Canceled)

159. (Previously presented) The process of claim 155, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to 3×10^5 Daltons, and a bead diameter of 20-40 μm.

160. (Previously presented) The process of claim 159, wherein the gel permeation chromatography column is Superose 12.

161. (Previously amended) The process of claim 155, wherein in the molecular weight markers the molar fraction of alanine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

162. (Previously amended) The process of claim 161, wherein in the molecular weight markers the molar fraction of alanine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

163. (Previously presented) The process of claim 155, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and

AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

164. (Previously presented) The process of claim 155, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

REMARKS

Claims 123, 127-134, 138-145, 149-155 and 159-164 were pending in the subject application. By this Amendment, applicants have amended claims 123 and 144. Accordingly, claims 123, 127-134, 138-145, 149-155 and 159-164 are pending in the subject application.

Support for the amendment to claim 123 may be found *inter alia* on page 3, lines 28-31 of the subject application.

Support for the amendment to claim 144 may be found *inter alia* in column 2, lines 40-43 of U.S. Patent No. 5,800,808, the relevant text of which has been incorporated into the subject application by this amendment and on page 32, lines 15-16 of the subject application.

Initially, applicants thank Examiner P. Huynh for scheduling a telephone conference with the undersigned at 1 p.m. on Tuesday, July 26, 2005. Applicants hope the following remarks overcome the rejections of record, but to the extent the Examiner has further questions, such can be addressed during the July 26 telephone conference.

Rejection under 35 U.S.C. §102(a)

On page 2, section 5 of the June 16, 2005 Final Office Action, the Examiner maintained the rejection of claims 123, 127-128, 133-134, 138-139, 144-145, 149-150, 155 and 159-160 under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 5,800,808 ("the '808 patent") as evident by the Pharmacia Biotech Directory, citing pages 340-341.

The Examiner alleged that the '808 patent teaches a process for obtaining a pharmaceutical product containing an aqueous mixture of polypeptides each of which consists of essentially of alanine, glutamic acid, tyrosine and lysine wherein the reference mixture has a desired average molecular weight of about 4,000-8,600 Dalton which is within the claimed average molecular weight from 4000 to 13,000 Daltons, citing col. 2, lines 8-14, in particular. The Examiner also alleged that during the process, a batch of the reference aqueous mixture of polypeptides is chromatograph on a column to such as Fractogel TSK and Superose 12 column, citing col. 3, line 6-8, to establish a relationship between retention time on the column and the molecular weight (see paragraph bridging cols 2-3, in particular). The Examiner further alleged that the reference's Superpose 12 column inherently comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to 3×10^5 Daltons and a bead diameter of 20-40 μm based on average molecular weight of the reference 4,000-8,600 Daltons which is within the claimed average molecular weight from 4000 to 13,000 Daltons and as evident by evidentiary reference Pharmacia Biotech Directory, citing page 341, in particular. The Examiner also alleged that the reference's process of obtaining the reference pharmaceutical product is by column chromatography of L-GLAT to obtain the desired average of molecular weight species, citing the Summary of Invention section, in particular.

In response, applicants maintain that the '808 patent does not anticipate the applicants' invention. Column 3, lines 6-8 of the '808 patent states, "[T]he molecular distribution

of the 2 batches was determined on a calibrated gel filtration column (Superose 12)." No reference to "markers", much less to the specific polypeptide markers of applicants' invention, is made in the '808 patent.

Applicants reiterate that the calibration step of the claimed invention uses a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence.

Applicants point out that a gel filtration column may be calibrated in any number of ways. For example, applicants attach hereto as **Exhibit 1** a list of calibration kits sold by the maker of the Superose 12 column (now GE Healthcare). None of the markers in the polypeptide kits are made from only four distinct amino acids, let alone the four specified in applicants' invention.[1]

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. §2131 (citing Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987)) The '808 patent does not disclose the characteristics of the molecular weight markers used, let alone teach the use of molecular weight markers consisting essentially of the four specified amino acids. As such, the '808 patent does not anticipate the applicants' invention.

[1] For example, ribonuclease A, the sequence of which is attached in **Exhibit 2**, contains many more than four amino acids.

Accordingly, applicants request that the Examiner reconsider and withdraw the rejection of claims 123, 127-128, 133-134, 138-139, 144-145, 149-150, 155 and 159-160 under 35 U.S.C. §102(b) as allegedly anticipated by the '808 patent.

Rejection under 35 U.S.C. §102(e)

On page 3, section 6 of the June 16, 2005 Final Office Action, the Examiner maintained the rejection of claims 123, 133-134 and 144 under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,858,964 ("the '964 patent").

The Examiner alleged that the '964 patent teaches a process for obtaining a pharmaceutical product containing an aqueous mixture of polypeptides each of which consists of essentially of alanine, glutamic acid, tyrosine and lysine wherein the reference mixture has a desired average molecular weight of about 4,000-12,000 which is within the claimed average molecular weight from 4000 to 13,000 Daltons, citing the Summary of Invention section, col.3, lines 1-4, in particular. The Examiner alleged that the reference's process of obtaining the reference pharmaceutical product is by column chromatography of L-GLAT to obtain the desired average of molecular weight species, citing column 4, lines 8-10. The Examiner also alleged that the step of calibrating the molecular weight obtained using the column chromatography is inherent in the reference process given that the reference method produces the same desire molecular weight. The Examiner further alleged that the reference polypeptide is copolymer-1, which is also known as glatiramer acetate, citing column 2, lines 18-21. The Examiner also alleged that the reference's process

further comprises a step of lyophilized the reference glatiramer acetate, citing column 4, line 35-36. Thus, the Examiner concluded that the reference teachings anticipate the claimed invention.

In response, applicants maintain that the '964 patent does not anticipate the applicants' invention. No reference to calibration, much less to "markers" or the specific polypeptide markers of applicants' invention, is made in the '964 patent.

Applicants reiterate that the calibration step of the claimed invention uses a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence.

Applicants point out that a gel filtration column may be calibrated in any number of ways. For example, applicants attach hereto as **Exhibit 1** a list of calibration kits sold by the maker of the Superose 12 column (now GE Healthcare). None of the markers in the polypeptide kits are made from only four distinct amino acids, let alone the four specified in applicants' invention.[2]

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. §2131 (citing Verdegaal Bros. v. Union Oil Co. of

[2] For example, ribonuclease A, the sequence of which is attached in **Exhibit 2**, contains many more than four amino acids.

California, 814 F.2d 628, 631 (Fed. Cir. 1987)) The '964 patent does not disclose the characteristics of the molecular weight markers used, let alone teach the use of molecular weight markers consisting essentially of the four specified amino acids. As such, the '964 patent does not anticipate the applicants' invention.

Accordingly, applicants request that the Examiner reconsider and withdraw the rejection of claims 123, 133-134 and 144 under 35 U.S.C. §102(e) as allegedly anticipated by the '964 patent.

Rejection under 35 U.S.C. §103(a)

On page 4, section 9 of the June 16, 2005 Final Office Action, the Examiner maintained the rejection of claims 123, 127-128, 134, 138-139, 145, 149-150, 155, and 159-160 under 35 U.S.C. 103(a) as allegedly unpatentable over the '964 patent in view of Pharmacia Biotech Directory, citing pages 340-341. The Examiner stated the teachings of the '964 patent have been discussed supra.

The Examiner alleged that the invention in claims 127, 138, 149 and 159 differs from the teachings of the references only in that the process for obtaining a pharmaceutical product wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to 3×10^5 Daltons and a bead diameter of 20-40 μm.

The Examiner alleged that the invention in claims 128, 139, 150, and 160 differs from the teachings of the references

only in that the process for obtaining a pharmaceutical product wherein the gel permeation chromatography column is Superose 12.

The Examiner also alleged that Pharmacia Biotech Directory teaches a process of separating peptide based on sized using a Superose column such as Superpose 12 that is a media that provides high resolution gel filtration at rapid flow rates in a wide range of buffer conditions, citing page 340, column 1. The Examiner further alleged that the reference gel permeation chromatography column is a cross-linked agarose-based medium with an exclusion limit of 2×10^6 Daltons, and has an optimal separation range of 1000 to 3×10^5 Daltons and a bead diameter of 20-40 μm citing page 341, far right column. The Examiner alleged that the reference further teaches that the highly cross-linked agarose structure of Superose is suitable for separation, purification and molecular weight determination of proteins, peptides and nucleic acid, citing page 340, column 1, first paragraph.

The Examiner alleged it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chromatography column as taught by the '964 patent for the Superose column as taught by Pharmacia Biotech Directory for a method of obtaining a pharmaceutical product based on size exclusion as taught by the '964 patent and Pharmacia Biotech Directory. The Examiner also alleged that from the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

The Examiner also alleged that one having ordinary skill in the art would have been motivated to do this because the Pharmacia Biotech Directory teaches that the highly cross-linked agarose structure of Superose is suitable for separation, purification and molecular weight determination of proteins, peptides and nucleic acids, citing page 340, column 1, first paragraph. The Examiner further alleged that the '964 patent teaches the desired average of molecular weight of copolymer-1 or glatiramer acetate that consists of essentially of alanine, glutamic acid, tyrosine and lysine as a pharmaceutical product is about 4,000-12,000 which is within the claimed average molecular weight from 4000 to 13,000 Daltons, citing the Summary of Invention section, column 3, lines 1-4.

In response, applicants point out that neither the '964 patent nor Pharmacia Biotech Directory alone or in combination teaches or suggests use of a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence, to calibrate a gel filtration column. As such, one skilled in the art would have no motivation to use, nor any expectation of success of using, a plurality of molecular weight markers of the subject invention for the calibration of a chromatography column based on the disclosures of the '964 patent and Pharmacia Biotech Directory.

As noted previously, the calibration step of the claimed invention uses a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine,

glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence. No motivation exists in the prior art for using such molecular weight markers. Furthermore, absent hindsight, the prior art offered no expectation of success of doing so. Yet furthermore, the art in any combination fails to teach every element of applicants' claims, *e.g.*, the markers as recited in applicants' claims are not taught in any of the cited art. Indeed, the Examiner has not offered any evidence to the contrary. Therefore, applicants' invention is not obvious over the '964 patent in view of Pharmacia Biotech Directory.

Accordingly, applicants request that the Examiner reconsider and withdraw the rejection of claims 123, 127-128, 134, 138-139, 145, 149-150, 155, and 159-160 under 35 U.S.C. §103(a) as being unpatentable over the '964 patent in view of Pharmacia Biotech Directory.

Allowable Subject Matter

On page 6, section 10 of the June 16, 2005 Final Office Action, the Examiner maintained the objection to claims 129-132, 140-143, 151-154 and 161-164 as being dependent upon a rejected base claim. However, the Examiner stated that these claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

As discussed above, the rejections of base claims should be withdrawn. Applicants therefore request that the Examiner reconsider and withdraw the objections of claims 129-132, 140-143, 151-154 and 161-164.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Gary J. Gershik 7/18/05

John P. White Date
Reg. No. 28,678
Gary J. Gershik
Reg. No. 39,992